

REMARKS

Entry of this Amendment is proper under 37 C.F.R. § 1.116 because the Amendment places the application in condition for allowance for the reasons discussed herein; and does not raise any new issues requiring further search and/or consideration. Entry of the Amendment is thus respectfully requested.

Claims 1-5, 7-9 and 11-12 are currently pending. Claim 2 is amended herein to address an issue of antecedent basis. Claim 4 is amended herein to correct a typographical error. Thus, no new matter is presented by way of the present Amendment.

Claim Objections

Claim 4 is objected to for the recitation of "I-6". Claim 4 is amended herein to replace "I-6" with "IL-6". Thus, this objection is obviated.

Rejections Under 35 U.S.C. § 112

Claim 2 stands rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite, for the recitation of the phrase "said ligand". Specifically, this term purportedly lacks antecedent basis. Claim 2 is amended herein to provide antecedent basis. Thus, Applicants request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 1-4 and 7-12 stand rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Sui et al. (*PNAS*, Vol. 92 (1995)) and further in view of Wong et al. (WO 96/04314). Sui et al. is cited for purportedly disclosing the administration of the

IL-6/IL-6R complex. Wong et al. is cited for purportedly disclosing that it is advantageous to make fusion proteins. The Office Action states that it would have been *prima facie* obvious to the skilled artisan to make a fusion protein, as disclosed by Wong et al., comprising IL-6 and IL-6R, because administration of a IL-6/IL-6R complex along with SCF increases expansion of progenitor cells, as disclosed by Sui et al. Applicants respectfully traverse.

As set forth in M.P.E.P § 2142, in order to establish a *prima facie* case of obviousness, three criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art references must teach or suggest all the claim limitations. Applicants submit that these criteria are not met by the cited references, alone or in combination.

Independent claim 1 of the present invention is directed to a conjugate comprising two polypeptides, wherein one polypeptide is a cytokine receptor or subunit thereof, and the other polypeptide is a cytokine or subunit thereof, that binds to the cytokine receptor. The polypeptides are linked to each other via a polypeptide linker.

Sui et al. disclose that the application of IL-6 and IL-6R, as well as SCF, results in the stimulation of the expansion of hemotopoietic precursor cells and CD34+ cells, respectively (see the abstract, page 2860 and Figure 1 of Sui). Because IL-6 and IL-6R are used separately in Sui et al, this reference does not disclose the claimed conjugate of the present invention.

Wong et al , the secondary reference, disclose a MHC molecule, which is covalently bound to the peptide. The peptide is presented via a peptide linder. The MHC molecule is used for modifying the activity of particular T-cells (see abstract and page 13, lines 11 to 13 of Wong). However, the MHC molecule of Wong does not correspond to a cytokine receptor. Nor does the peptide of Wong correspond to a cytokine. Thus, Wong et al. does not disclose the conjugate of the present invention.

Neither of the cited references disclose or even suggest a conjugate comprising two polypeptides, one polypeptide being a cytokine receptor, or a subunit thereof, and the other polypeptide being a cytokine, or a submit thereof that binds to said cytokine receptor, wherein the polypeptides are linked to each other via a polypeptide linker, as claimed in the present invention. Thus, the cited references fail to recite each element of the claimed invention.

Further, there is no motivation to modify the cited references to arrive at the claimed invention, or any expectation of success for the skilled artisan to attempt it. To this end, Applicants submit that Sui fails to recite or even suggest the fusion polypeptide of the present invention. Sui et al merely reflects the state of the art prior to the present invention, as it discloses the separate application of IL-6 and its receptor. This separate application is disadvantageous, and in fact is a problem addressed by the present invention.

Applicants submit that Wong et al. relates to a field of study which does not relate to the field of the present invention. In fact, Wong et al. does not describe the fusion of a receptor to its ligand. Rather, Wong et al. merely disclose the activation of T-cells by use of a complex of a surface antigen of a cell and a peptide.

Furthermore, the process disclosed in Wong does not relate to the processes of the present invention. Thus, the skilled artisan, in attempting to find a solution to the problem solved by the present invention, *i.e.*, the elimination of the disturbed interaction between proteins would not consider Wong et al. Thus, Wong fails to remedy the deficiencies of Sui, and neither reference provides an incentive for the skilled artisan to generate the fusion polypeptide of the present invention.

Finally, Applicants respectfully submit that unexpected results are present with respect to the present invention. It is a well established legal precedent that the presence of an unexpected, advantageous or superior result is evidence of nonobviousness. See M.P.E.P. § 716.02(a); *In re Papesch*, 315 F.2d 381, 137 U.S.P.Q. 43 (C.C.P.A. 1963). Along these lines, it is also well established that "a greater than expected result" is evidence of nonobviousness. See M.P.E.P. § 716.02(a); *In re Corkill*, 711 F.2d 1496, 226 U.S.P.Q. 1005 (Fed. Cir. 1985). Applicants submit that the fusion protein of the present invention provides surprising and unexpected results.

Specifically, Applicants submit that it was surprising discovered that by use of the fusion polypeptide of the present invention, the effects of the single polypeptides were dramatically increased. To this end, Applicants refer to Example 5 of the present specification, which show that the expansion of the colony formation of CD34+ cells can be increased by 300% compared to the separate addition of IL-6 and IL-6 receptor.

Further, Example 4 of the specification shows that through the use of the fusion polypeptide of the present invention, the haptoglobin expression in a hepatoma cell line is stimulated to a greater extent as compared to that resulting

from the separate addition of IL-6 and IL-6R. In further support, Applicants submit that the fusion polypeptide of the present invention is capable of regenerating diseased liver tissue which can not be achieved by application of the single polypeptide.

Thus, the fusion polypeptide of the present invention provides a new group of compounds which surprisingly and for the first time, eliminate any disturbed interaction between proteins. Thus, the claims are patentable over the cited references, and Applicants respectfully request that the rejections be withdrawn.

CONCLUSION

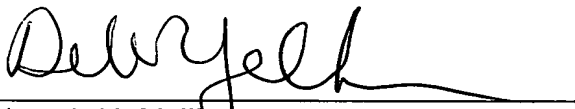
In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

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By: 

Deborah H. Yellin
Registration No. 45,904

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620